Claim 82 has been canceled, claims 57-81 and 83-103 have been amended and claim 104 has been added. Applicant submits that these amendments and additions are fully supported by the specification and do not present new matter.

Specifically, claims 57-81 and 83-103 have been amended to correct claim dependency and find support *inter alia* in original claims 57-103.

In addition, claims 57 and 58, as amended, include the language that the inventive method is high-throughput and that the plurality of reaction vessels comprises at least 96 reaction vessels. Support for such language can be found throughout the specification, for example, on page 29 lines 6-19, where it is described that 96-well plates, or higher density arrays (*e.g.*, 384- or 1536-well plates), can be used to practice the present invention.

Claims 72 and 73, as amended, incorporate language that more particularly points out what Applicant regards as his invention with respect to the language "one or more solutions containing at least one reagent". Applicant notes that claim 72 now recites "*one reagent characterized in that, when contacted with the cells, it perturbs or functions as an indicator of the intracellular biological or chemical process*". Similarly, claim 73 now includes the language that "*contacting the cells with ... for the reagent to perturb or function as an indicator of the intracellular biological or chemical process in the cells*". Applicant respectfully submits that such language is fully supported by the specification. Support for such language can be found, for example, in Figures 7 and 9-11 and Examples 6-10 (pages 61-65) where it is described that a reagent (*e.g.*, rapamycin or nocodazole) that perturbs an intracellular biological or chemical process of interest (*e.g.*, DNA synthesis or cell mitosis, respectively) may be contacted with the cells to identify test compounds that exert an effect on the perturbed intracellular biological or chemical process. Additional support can be found on page 30 lines 22-24, page 31 lines 1-12, in Figures 1-4, 8, 11c-d and in Examples 1-3, 6-7 (pages 48-63), where it is detailed that a reagent (*e.g.*, BrdU) that functions as an indicator of an intracellular biological or chemical process of interest (*e.g.*, cell growth and viability) may be contacted with the cells to identify test compounds that exert an effect on the intracellular biological or chemical process (*e.g.*, DNA synthesis).

Newly amended claim 74 includes the language that "*the reagent is a natural or non-natural nucleotide*". Support for such amendment can be found, for example, in the paragraph bridging pages 30 and 31 (*e.g.*, line 2 page 31).

Claim 78 no longer includes reference to a biochemical reaction. No new matter is added with this amendment.

Newly amended claim 79 finds support *inter alia* in original claim 79 and in (now canceled) claim 82.

Support for newly amended claim 88 and newly added claim 104 can be found *inter alia* in original claims 31-33 and throughout the specification, for example, in the section entitled "Test Compounds" on pages 39-40 of the specification, where it is recited that compounds may be obtained from natural or synthetic sources.

Newly amended claims 95-98 find support *inter alia* in original claims 95-98 and in the specification, for example, on page 29 lines 1-5.

Applicant respectfully submits that claim amendments, as described above and detailed herein, do not present new matter, and Applicant thus respectfully requests entry of these amendments, and consideration of these amendments in the following remarks.

Rejections under 35 U.S.C. § 112, ¶ 2

A. The Examiner has rejected claims 57 and 58 under 35 U.S.C. § 112, second paragraph and states that the language "characterized by an ability to associate intracellularly with a biological component…" is not clear. The cited language is not present in newly amended claims 57 and 58, therefore the stated rejection is now moot. Applicant notes that claims 57 and 58 now recite that the ligand "is characterized *in that it associates intracellularly* with a biological component…", and respectfully submits that such language is perfectly clear in view of the specification. Specifically, one of ordinary skill in the art would understand that the ligand, as used according to the claimed invention, binds intracellularly with a biological component.

B. The Examiner has rejected claim 62 for reciting a limitation on a "*third ligand*", which the Examiner states is not required in claim 58 from which claim 62 depends. Applicant respectfully notes that antecedent basis for "*third ligand*" can be implicitly found in step g of

claim 58 in the language "*wherein seconds are thirds*". The language is intended to mean that every occurrence of the word "second" in steps d-f is replaced with the word "third". Thus, the language "second ligand" found in steps d-f becomes "third ligand" in step g. Therefore, the language "third ligand" in claim 62 properly finds antecedent basis in claim 58 from which claim 62 depends.

C. The Examiner has rejected claim 66 for reciting the limitation that the secondary ligand is assayed intracellularly. Specifically, the Examiner states that it is not clear how claim 66 further limits claims 64 and 65 because the first ligand to which the secondary ligand is bound appears to be present intracellularly. Applicant respectfully submits that claim 66 is directed to an embodiment whereby the biological component-associated secondary ligand may be detected while still in the cell (*i.e.*, intracellular detection), as opposed to lysing the cells prior to detecting the component-associated secondary ligand (*i.e.*, extracellular detection). Therefore, claim 66 properly limits the claims from which it depends.

D. The Examiner has rejected claim 72 found reciting the language "one reagent to exert an effect", which the Examiner found was unclear. The cited language is not present in newly amended claim 72, therefore the rejection is now moot. Applicant notes that claim 72 now recites "*one reagent characterized in that, when contacted with the cells, it perturbs or functions as an indicator of the intracellular biological or chemical process*", and respectfully submits that such language is perfectly clear in view of the specification. Support for such language can be found, for example, in Figures 7 and 9-11 and Examples 6-10 (pages 61-65) where it is described that a reagent (*e.g.*, rapamycin or nocodazole) that perturbs an intracellular biological or chemical process of interest (*e.g.*, DNA synthesis or cell mitosis, respectively) may be contacted with the cells to identify test compounds that exert an effect on the perturbed intracellular biological or chemical process. Additional support can be found on page 30 lines 22-24, page 31 lines 1-12, in Figures 1-4, 8, 11c-d and in Examples 1-3, 6-7 (pages 48-63), where it is detailed that a reagent (*e.g.*, BrdU) that functions as an indicator of an intracellular biological or chemical process of interest (*e.g.*, DNA synthesis) may be contacted with the cells to identify test compounds that exert an effect on the intracellular biological or chemical process.

E. The Examiner has rejected claim 78 for indefiniteness. Specifically, the Examiner states that the difference between an "intracellular biological reaction" and an

"intracellular biochemical reaction" is not clear. Applicant notes that newly amended claim 78 does not include the language which is objected to, therefore the rejection is now moot.

F. The Examiner has rejected claim 82 and states that it is not clear how it further limits claim 79. Claim 82 has been canceled and the corresponding subject matter has been incorporated into newly amended claim 79. Therefore the rejection is now moot.

G. The Examiner has rejected claim 88 for failure to further limit claims 57 and 58 from which it depends. Newly amended claim 88 now recites that at least one test compound may be from a synthetic source. Applicant respectfully submits that newly amended claim 88 properly limits claims 57 and 58.

H. The Examiner has rejected claims 95-98 for indefiniteness. Specifically, the Examiner states that the density of reaction vessels cannot be interpreted without any specified arrangement of vessels relative to another. In an effort to expedite prosecution, and without conceding the correctness of the Examiner's position, Applicant has amended claims 95-98 to include language pertaining to the spatial arrangement of vessels. Applicant respectfully submits that claims 95-98, as amended, are clear to one of ordinary skill in the art.

In view of the amendments detailed above, Applicant asserts that the claims, as amended, particularly point out and distinctly claim the invention, and respectfully requests that the rejections under 35 U.S.C. § 112, second paragraph be withdrawn.

Rejections under 35 U.S.C. § 102(a), (b) and (e)

1. Claims 57-62, 69-78, 83, 85-88, 102 and 103 are rejected under 35 U.S.C. § 102(e) as being anticipated by Walsh (U.S. patent 5,990,092);

2. Claims 57, 59-61, 64, 66, 67, 69, 71-74, 76-79, 81-83, 85-88, 102 and 103 are rejected under 35 U.S.C. § 102(b) as being anticipated by Photiou *et al.* (European Journal of Cancer, 33(3):463-470, March 1997);

3. Claims 57-62, 64-67, 69-83, 85-88, 102 and 103 are rejected under 35 U.S.C. § 102(a) as being anticipated by Juan *et al.* (Experimental Cell Research, 239:104-110, February 1988); and

4. Claims 57-62, 64-67, 69-83, 85-88, 102 and 103 are rejected under 35 U.S.C. § 102(a) as being anticipated by Claycomb (U.S. patent 6,316,207 B1; PCT published May 1998).

Applicant notes that none of the cited references teach a *high-throughput* method for screening test compounds to identify those that exert an effect on an intracellular biological or chemical process, wherein the method comprises steps of introducing into each of a plurality of reaction vessels (i) a plurality of cells, (ii) one or more test compounds, and (iii) a first ligand; and (iv) assaying for ligand-component association in the reaction vessels; *wherein the plurality of reaction vessels comprises at least 96 reaction vessels.*

Specifically, Claycomb teaches a cell proliferation assay using BrdU labeling, where the cells are plated on coverslips in *12-well plates* in *1 ml* of suitable medium. Photiou *et al.* teach an indirect immunofluorescence assay where the cells are plated on coverslips in *24-well plates.* Neither the Walsh nor the Juan *et al.* reference specifically teaches *high-throughput* screening methods (*e.g.*, number of reaction vessels ≥ 96) according to the claimed invention. In fact, the *in vitro* assay of Example 4 in the Walsh reference (column 28 lines 47-57) which the Examiner refers to in his Office Action, describes that the "cells are fixed onto *the tissue culture dish* and dried overnight at 37°C and immunostained..." Thus, the method disclosed in the Walsh reference only utilizes *one* reaction vessel (*i.e.*, a tissue culture dish). None of the cited references teach that the cell-based assays in question can be carried out in high-throughput format (*e.g.*, with 96 or higher reaction vessels) not do they provide any teaching as to how this might be accomplished.

Therefore the cited references cannot anticipate the presently claimed invention. Applicant respectfully requests that each of the stated rejections under 35 U.S.C. § 102(a), (b) and (e) be withdrawn.

Rejection under 35 U.S.C. § 103

Claims 89-101 are rejected under 35 U.S.C. § 103(a) as being unpatentable over any one or more of Walsh, Photiou *et al.*, Juan *et al.*, Claycomb and the Final Conference Program of LabAutomation '98 in San Diego, CA January 17-21, 1998, pages 99, 100, 124, 129 and 212.

The Examiner concedes that the cited references do not explicitly teach test compounds from a combinatorial library, the release of test compounds from a solid support, *or various capacities and densities of wells in well plates.* In fact, none of the Walsh, Photiou *et al.*, Juan *et*

al., Claycomb references teach a *high-throughput* method for screening test compounds to identify those that exert an effect on an intracellular biological or chemical process, wherein the method comprises steps of introducing into each of a plurality of reaction vessels (i) a plurality of cells, (ii) one or more test compounds, and (iii) a first ligand that associates intracellularly with a biological component of interest; and (iv) assaying for ligand-component association in the reaction vessels; *wherein the plurality of reaction vessels comprises at least 96 reaction vessels.*

Specifically, as discussed above, Claycomb teaches a cell proliferation assay using BrdU labeling, where the cells are plated on coverslips in *12-well plates* in *1 ml* of suitable medium. Photiou *et al.* teach an indirect immunofluorescence assay where the cells are plated on coverslips in *24-well plates*. Neither the Walsh nor the Juan *et al.* reference specifically teaches high-throughput screening methods (*e.g.*, number of reaction vessels ≥ 96) according to the claimed invention. In fact, the *in vitro* assay of Example 4 in the Walsh reference (column 28 lines 47-57) which the Examiner refers to in his Office Action, describes that the "cells are fixed onto *the tissue culture dish* and dried overnight at 37°C and immunostained..." Thus, as discussed previously, the method disclosed in the Walsh reference only utilizes *one* reaction vessel. None of the Walsh, Photiou *et al.*, Juan *et al.*, Claycomb references teach or suggest that the cell-based assays in question can be carried out in high-throughput format (*e.g.*, with 96 or higher reaction vessels) not do they provide any teaching or suggestion as to how this might be accomplished.

In addition, while the "Final Conference Program of LabAutomation '98" reference provides examples of the use of 96-, 384-, 1536- and 10,000-well plates in enzymatic fluorescent kinetic assays (see page 100), Applicant fails to find any teaching or suggestion in that reference that these high density plates (*i.e.*, 96-, 384-, 1536- and 10,000-well plates) can be used in a *high-throughput* method for screening test compounds to identify those that exert an effect on an intracellular biological or chemical process, wherein the method comprises steps of introducing into each of a plurality of reaction vessels (i) a plurality of cells, (ii) one or more test compounds, and (iii) a first ligand that associates intracellularly with a biological component of interest; and (iv) assaying for ligand-component association in the reaction vessels.

Furthermore, Applicant submits that there is no teaching, suggestion or incentive in any of the cited references to combine the teachings of the "Final Conference Program of LabAutomation '98" reference with any one or more of the Walsh, Photiou *et al.*, Juan *et al.* and Claycomb references to achieve the presently claimed invention. In fact, the "Final Conference Program of LabAutomation '98" reference teaches that "*some cell-based assays remain difficult to automate due to the incompatibility of traditional assay platforms with robotics*" (see page 159, first paragraph). Therefore, Applicant argues that the "Final Conference Program of LabAutomation '98" reference actually *teaches away* from the presently claimed invention, in that it fails to convey to one of ordinary skill in the art the desirability to combine the teachings of the cited references and a reasonable expectation of success in such combination. Hence, Applicant argues that one of ordinary skill in the relevant art would *not* have been motivated to combine the teachings of the cited references to achieve the presently claimed invention, at the time the invention was made, because there was no reasonable expectation of success. Applicant emphasizes that the mere fact that the references *can* be combined does not establish a *Prima Facie* case of obviousness: the desirability of the combination *must* be suggested in the prior art (*In re* Kotzab, 55 USPQ2d 1313, Fed. Cir. 2000).

In view of the remarks above, Applicant respectfully submits that the Examiner has failed to establish a *Prima Facie* case of obviousness, because there is no teaching, suggestion or motivation in any of the cited references to combine the teachings of Walsh, Photiou *et al.*, Juan *et al.*, Claycomb and the Final Conference Program of LabAutomation '98 reference to achieve the claimed invention. Therefore, claims 89-101 cannot be held obvious over any one or more of Walsh, Photiou *et al.*, Juan *et al.*, Claycomb in view of the Final Conference Program of LabAutomation '98 reference.

In light of the present Amendment and Remarks, Applicant respectfully submits that the present case is in condition for allowance. A Notice to that effect is respectfully requested.

Please charge any fees that may be associated with this matter, or credit any overpayments, to our Deposit Account No. 03-1721.

Respectfully submitted

Date: May 19, 2003

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on May 19, 2003
Kathy Hartgoga

- APPENDIX A –

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claim Replacements:

57. A high-throughput method for screening one or more test compounds to identify those that exert an effect on an intracellular biological or chemical process, the method comprising steps of:

    a. introducing into each of a plurality of reaction vessels:

       a plurality of cells; and

       one or more test compounds whose effect on an intracellular biological or chemical process is to be evaluated;

    b. introducing into each of the reaction vessels a first ligand characterized [by an ability to associate] in that it associates intracellularly with a biological component whose presence or amount reveals the effect of a given test compound on the biological or chemical process; and

    c. assaying for ligand-component association in the reaction vessels;

wherein the plurality of reaction vessels comprises at least 96 reaction vessels.

58. A high-throughput method for screening one or more test compounds; said method comprising steps of:

    a. introducing into each of a plurality of reaction vessels:

       a plurality of cells; and

       one or more test compounds whose effect on an intracellular biological or chemical process is to be evaluated;

    b. introducing into each of the reaction vessels a first ligand characterized [by an ability to associate] in that it associates intracellularly with a biological component whose presence or amount reveals the effect of a given test compound on the biological or chemical process;

c. assaying for association between the first ligand and the component in the reaction vessels;

d. repeating step a;

e. introducing into each of the reaction vessels a second ligand characterized [by an ability to associate] <u>in that it associates</u> intracellularly with a biological component whose presence or amount reveals the effect of a given test compound on the biological or chemical process;

f. assaying for association between the second ligand and the component in the reaction vessels;

g. optionally repeating steps d-f, wherein seconds are thirds; and

h. retaining the information as a functional fingerprint;

<u>wherein the plurality of reaction vessels comprises at least 96 reaction vessels.</u>

59. The method of claim [82 or 83] <u>57 or 58</u> further comprising the step of removing unassociated ligand from each reaction vessel.

60. The method of claim [82 or 83] <u>57 or 58</u> wherein the biological component is a direct participant in or a product of the biological or chemical process.

61. The method of claim [82] <u>57</u> wherein the ligand is an antibody.

62. The method of claim [83] <u>58</u> wherein each first, second and third ligand is independently an antibody.

63. The method of claim [86 or 87] <u>61 or 62</u> wherein the antibody is conjugated to horseradish peroxidase.

64. The method of claim [82] <u>57</u> wherein the method further comprises introducing a secondary ligand that binds specifically to said first ligand, and wherein the step of assaying comprises assaying for bound secondary ligand.

65. The method of claim [83] <u>58</u> wherein the method further comprises introducing a secondary ligand that binds specifically to said first, second or third ligand, and wherein each step of assaying comprises assaying for bound secondary ligand.

66. The method of claim [89 or 90] <u>64 or 65</u> wherein in the step of assaying, the secondary ligand is assayed intracellularly.

67. The method of claim [89 or 90] <u>64 or 65</u> wherein the secondary ligand is an antibody.

68. The method of claim [92] <u>67</u> wherein the antibody is conjugated to horseradish peroxidase.

69. The method of claim [82 or 89] <u>57 or 64</u> wherein the step of assaying utilizes a detection technique selected from the group consisting of: chemiluminescence, fluorescence, phosphorescence, radioactivity, colorimetry, Ultra-Violet spectroscopy, and Infra-Red spectroscopy.

70. The method of claim [83 or 90] <u>58 or 65</u> wherein each step of assaying independently utilizes a detection technique selected from the group consisting of: chemiluminescence, fluorescence, phosphorescence, radioactivity, colorimetry, Ultra-Violet spectroscopy, and Infra-Red spectroscopy.

71. The method of claim [82 or 83] <u>57 or 58</u> wherein, in the step of introducing the cells in each of the plurality of reaction vessels, the cells adhere to the reaction vessel surface.

72. The method of claim [82 or 83] <u>57 or 58</u> further comprising the step of providing one or more solutions containing at least one reagent <u>characterized in that, when contacted with the cells, it perturbs or functions as an indicator of</u> [to exert an effect on] the intracellular biological or chemical process.

73. The method of claim [97] 72 further comprising the step of contacting the cells with the one or more solutions under suitable conditions for the reagent to [exert an effect on] perturb or function as an indicator of the intracellular biological or chemical process in the cells.

74. The method of claim [98] 73 wherein the intracellular biological or chemical process is DNA synthesis and the reagent comprises a natural or non-natural nucleotide.

75. The method of claim [98] 74 wherein the reagent is 5-bromodeoxyuridine.

76. The method of claim [82 or 83] 57 or 58 wherein the intracellular biological or chemical process is a covalent modification of an intracellular component.

77. The method of claim [101] 76 wherein the covalent modification is an intracellular biological reaction.

78. The method of claim [102] 77 wherein the intracellular biological reaction is nucleic acid synthesis, protein cleavage, peptide cleavage, carbohydrate addition, carbohydrate cleavage, metabolism of cellular [components, synthesis] components or synthesis of cellular components [or an intracellular biochemical reaction].

79. The method of claim [101] 76 wherein the covalent modification is a post-translational event and the intracellular component is a protein.

80. The method of claim [104] 79 wherein the post-translational event is protein glycosylation, methylation, lipidation, isoprenylation, ubiquitination, phosphorylation or acetylation.

81. The method of claim [104] 79 wherein the ligand interacts with the post-translationally modified intracellular component.

83. The method of claim [82 or 83] 57 or 58 wherein the cells are from the same cell –line.

84. The method of claim [82 or 83] 57 or 58 wherein the cells are from a plurality of cell – lines.

85. The method of claim [82 or 83] 57 or 58 wherein at least a subset of the cells comprises a eukaryotic cell.

86. The method of claim [82 or 83] 57 or 58 wherein at least a subset of the cells comprises a mammalian cell.

87. The method of claim [82 or 83] 57 or 58 wherein at least a subset of the cells comprises a human cell.

88. The method of claim [82 or 83] 57 or 58 wherein [the test compounds are] at least one test compound is from a [natural, biological or] synthetic source[, or combination thereof].

89. The method of claim [82 or 83] 88 wherein the test compounds are from a combinatorial library.

90. The method of claim [82 or 83] 89 wherein the test compounds are covalently bound on a solid support, the method further comprising the step of dissociating the test compounds from the solid support.

91. The method of claim [82 or 83] 57 or 58 wherein the reaction vessels are designed to receive a volume of liquid less or equal to approximately 200 microliters.

92. The method of claim [82 or 83] 57 or 58 wherein the reaction vessels are designed to receive a volume of liquid less or equal to approximately 50 microliters.

93. The method of claim [82 or 83] 57 or 58 wherein the reaction vessels are designed to receive a volume of liquid less or equal to approximately 2 microliters.

94. The method of claim [82 or 83] 57 or 58 wherein the reaction vessels are designed to receive a volume of liquid less or equal to approximately 250 nanoliters.

95. The method of claim [82 or 83] 57 or 58 wherein the reaction vessels are arranged in a two-dimensional array with sufficient density that the center-to-center distance between [individual] adjacent vessels [are separated from one another by no more than about 5 millimeters] is less than about 8.5 millimeters.

96. The method of claim [82 or 83] 57 or 58 wherein the reaction vessels are arranged in a two-dimensional array with sufficient density that the center-to-center distance between [individual] adjacent vessels [are separated from one another by no more than about 2 millimeters] is less than about 4.5 millimeters.

97. The method of claim [82 or 83] 57 or 58 wherein the reaction vessels are arranged in a two-dimensional array with sufficient density that the center-to-center distance between [individual] adjacent vessels [are separated from one another by no more than about 1 millimeters] is less than about 2.25 millimeters.

98. The method of claim [82 or 83] 57 or 58 wherein the reaction vessels are arranged in a two-dimensional array with sufficient density that the center-to-center distance between [individual] adjacent vessels [are separated from one another by no more than about 0.25 millimeters] is less than about 1 millimeter.

99. The method of claim [82 or 83] <u>57 or 58</u> wherein the number of reaction vessels is greater than or equal to approximately 384 and the reaction vessels occupy a surface smaller than or equal to approximately 128×86 mm^2.

100. The method of claim [82 or 83] <u>57 or 58</u> wherein the number of reaction vessels is greater than or equal to approximately 1500 and the reaction vessels occupy a surface smaller than or equal to approximately 128×86 mm^2.

101. The method of claim [82 or 83] <u>57 or 58</u> wherein the number of reaction vessels is greater than or equal to approximately 6000 and the reaction vessels occupy a surface smaller than or equal to approximately 128×86 mm^2.

102. The method of claim [82 or 83] <u>57 or 58</u> wherein in the step of introducing the test compounds into the plurality of reaction vessels, the test compounds are the same or different.

103. The method of claim [82 or 83] <u>57 or 58</u> wherein in the step of introducing the test compounds into the plurality of reaction vessels, each reaction vessel contains one test compound.

Paragraph Replacements:

<u>Paragraph on page 29 starting at line 1 and ending at line 5:</u>

According to the present invention, assays are preferably performed in dense arrays of reaction vessels. Preferably, the center-to-center distance between reaction vessels is less than about 8.5 [mM] <u>mm</u>. More preferably, the distance is less than 4.5 [mM] <u>mm</u>. Even more preferably the distance is less than approximately 2.25 [mM] <u>mm</u>. Most preferably, the distance is less than approximately 1 [mM] <u>mm</u>.

- APPENDIX B –

CLAIMS AS PENDING AFTER ENTRANCE OF THE PRESENT AMENDMENT

57. A high-throughput method for screening one or more test compounds to identify those that exert an effect on an intracellular biological or chemical process, the method comprising steps of:

a. introducing into each of a plurality of reaction vessels:

a plurality of cells; and

one or more test compounds whose effect on an intracellular biological or chemical process is to be evaluated;

b. introducing into each of the reaction vessels a first ligand characterized in that it associates intracellularly with a biological component whose presence or amount reveals the effect of a given test compound on the biological or chemical process; and

c. assaying for ligand-component association in the reaction vessels;

wherein the plurality of reaction vessels comprises at least 96 reaction vessels.

58. A high-throughput method for screening one or more test compounds; said method comprising steps of:

a. introducing into each of a plurality of reaction vessels:

a plurality of cells; and

one or more test compounds whose effect on an intracellular biological or chemical process is to be evaluated;

b. introducing into each of the reaction vessels a first ligand characterized in that it associates intracellularly with a biological component whose presence or amount reveals the effect of a given test compound on the biological or chemical process;

c. assaying for association between the first ligand and the component in the reaction vessels;

d. repeating step a;

e. introducing into each of the reaction vessels a second ligand characterized in that it associates intracellularly with a biological component whose presence or amount reveals the effect of a given test compound on the biological or chemical process;

f. assaying for association between the second ligand and the component in the reaction vessels;

g. optionally repeating steps d-f, wherein seconds are thirds; and

h. retaining the information as a functional fingerprint;

wherein the plurality of reaction vessels comprises at least 96 reaction vessels.

59. The method of claim 57 or 58 further comprising the step of removing unassociated ligand from each reaction vessel.

60. The method of claim 57 or 58 wherein the biological component is a direct participant in or a product of the biological or chemical process.

61. The method of claim 57 wherein the ligand is an antibody.

62. The method of claim 58 wherein each first, second and third ligand is independently an antibody.

63. The method of claim 61 or 62 wherein the antibody is conjugated to horseradish peroxidase.

64. The method of claim 57 wherein the method further comprises introducing a secondary ligand that binds specifically to said first ligand, and wherein the step of assaying comprises assaying for bound secondary ligand.

65. The method of claim 58 wherein the method further comprises introducing a secondary ligand that binds specifically to said first, second or third ligand, and wherein each step of assaying comprises assaying for bound secondary ligand.

66. The method of claim 64 or 65 wherein in the step of assaying, the secondary ligand is assayed intracellularly.

67. The method of claim 64 or 65 wherein the secondary ligand is an antibody.

68. The method of claim 67 wherein the antibody is conjugated to horseradish peroxidase.

69. The method of claim 57 or 64 wherein the step of assaying utilizes a detection technique selected from the group consisting of: chemiluminescence, fluorescence, phosphorescence, radioactivity, colorimetry, Ultra-Violet spectroscopy, and Infra-Red spectroscopy.

70. The method of claim 58 or 65 wherein each step of assaying independently utilizes a detection technique selected from the group consisting of: chemiluminescence, fluorescence, phosphorescence, radioactivity, colorimetry, Ultra-Violet spectroscopy, and Infra-Red spectroscopy.

71. The method of claim 57 or 58 wherein, in the step of introducing the cells in each of the plurality of reaction vessels, the cells adhere to the reaction vessel surface.

72. The method of claim 57 or 58 further comprising the step of providing one or more solutions containing at least one reagent characterized in that, when contacted with the cells, it perturbs or functions as an indicator of the intracellular biological or chemical process.

73. The method of claim 72 further comprising the step of contacting the cells with the one or more solutions under suitable conditions for the reagent to perturb or function as an indicator of the intracellular biological or chemical process in the cells.

74. The method of claim 73 wherein the intracellular biological or chemical process is DNA synthesis and the reagent comprises a natural or non-natural nucleotide.

75. The method of claim 74 wherein the reagent is 5-bromodeoxyuridine.

76. The method of claim 57 or 58 wherein the intracellular biological or chemical process is a covalent modification of an intracellular component.

77. The method of claim 76 wherein the covalent modification is an intracellular biological reaction.

78. The method of claim 77 wherein the intracellular biological reaction is nucleic acid synthesis, protein cleavage, peptide cleavage, carbohydrate addition, carbohydrate cleavage, metabolism of cellular components or synthesis of cellular components.

79. The method of claim 76 wherein the covalent modification is a post-translational event and the intracellular component is a protein.

80. The method of claim 79 wherein the post-translational event is protein glycosylation, methylation, lipidation, isoprenylation, ubiquitination, phosphorylation or acetylation.

81. The method of claim 79 wherein the ligand interacts with the post-translationally modified intracellular component.

83. The method of claim 57 or 58 wherein the cells are from the same cell –line.

84. The method of claim 57 or 58 wherein the cells are from a plurality of cell –lines.

85. The method of claim 57 or 58 wherein at least a subset of the cells comprises a eukaryotic cell.

86. The method of claim 57 or 58 wherein at least a subset of the cells comprises a mammalian cell.

87. The method of claim 57 or 58 wherein at least a subset of the cells comprises a human cell.

88. The method of claim 57 or 58 wherein at least one test compound is from a synthetic source.

89. The method of claim 88 wherein the test compounds are from a combinatorial library.

90. The method of claim 89 wherein the test compounds are covalently bound on a solid support, the method further comprising the step of dissociating the test compounds from the solid support.

91. The method of claim 57 or 58 wherein the reaction vessels are designed to receive a volume of liquid less or equal to approximately 200 microliters.

92. The method of claim 57 or 58 wherein the reaction vessels are designed to receive a volume of liquid less or equal to approximately 50 microliters.

93. The method of claim 57 or 58 wherein the reaction vessels are designed to receive a volume of liquid less or equal to approximately 2 microliters.

94. The method of claim 57 or 58 wherein the reaction vessels are designed to receive a volume of liquid less or equal to approximately 250 nanoliters.

95. The method of claim 57 or 58 wherein the reaction vessels are arranged in a two-dimensional array with sufficient density that the center-to-center distance between adjacent vessels is less than about 8.5 millimeters.

96. The method of claim 57 or 58 wherein the reaction vessels are arranged in a two-dimensional array with sufficient density that the center-to-center distance between adjacent vessels is less than about 4.5 millimeters.

97. The method of claim 57 or 58 wherein the reaction vessels are arranged in a two-dimensional array with sufficient density that the center-to-center distance between adjacent vessels is less than about 2.25 millimeters.

98. The method of claim 57 or 58 wherein the reaction vessels are arranged in a two-dimensional array with sufficient density that the center-to-center distance between adjacent vessels is less than about 1 millimeter.

99. The method of claim 57 or 58 wherein the number of reaction vessels is greater than or equal to approximately 384 and the reaction vessels occupy a surface smaller than or equal to approximately $128 \times 86\ mm^2$.

100. The method of claim 57 or 58 wherein the number of reaction vessels is greater than or equal to approximately 1500 and the reaction vessels occupy a surface smaller than or equal to approximately $128 \times 86\ mm^2$.

101. The method of claim 57 or 58 wherein the number of reaction vessels is greater than or equal to approximately 6000 and the reaction vessels occupy a surface smaller than or equal to approximately $128 \times 86\ mm^2$.

102. The method of claim 57 or 58 wherein in the step of introducing the test compounds into the plurality of reaction vessels, the test compounds are the same or different.

103. The method of claim 57 or 58 wherein in the step of introducing the test compounds into the plurality of reaction vessels, each reaction vessel contains one test compound.

104. The method of claim 57 or 58 wherein at least one test compound is from a natural source.